



TCA Cycle Pathway

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ILOs



***By the end of this lecture, students are
:expected to***

- 1. Illustrate the steps of tricarboxylic acid cycle.**
- 2. discuss the importance of tricarboxylic acid cycle.**
- 3. Calculate the ATP generated per each turn of the cycle.**
- 4. Enumerate the Anaploretic Reactions which replenish intermediates of TCA Cycle**



TCA cycle is also called

The Krebs Cycle

or

The Citric Acid Cycle

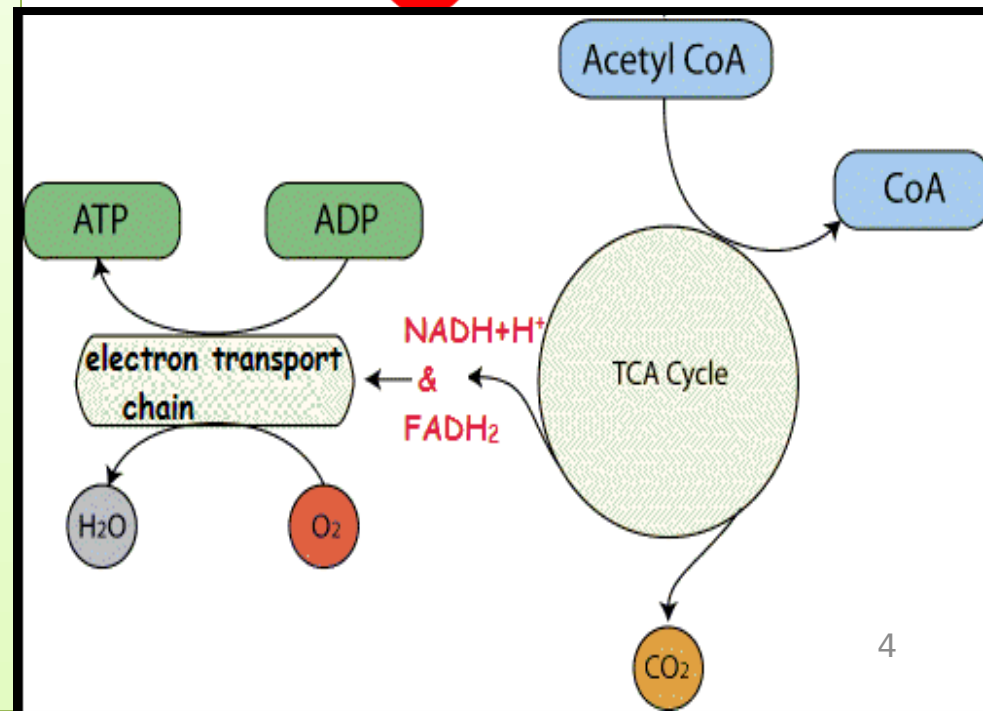
**It plays several roles in the
metabolism**

**TCA cycle occurs only in
mitochondrial matrix**

**By another meaning takes place
only in aerobic cell**

**Because its
products like
 $\text{NADH} + \text{H}^+$ &
 FADH_2**

**Must be reoxidized
back to NAD & FAD
BY electron
transport chain
which consume O_2
and produce ATP &
 H_2O**

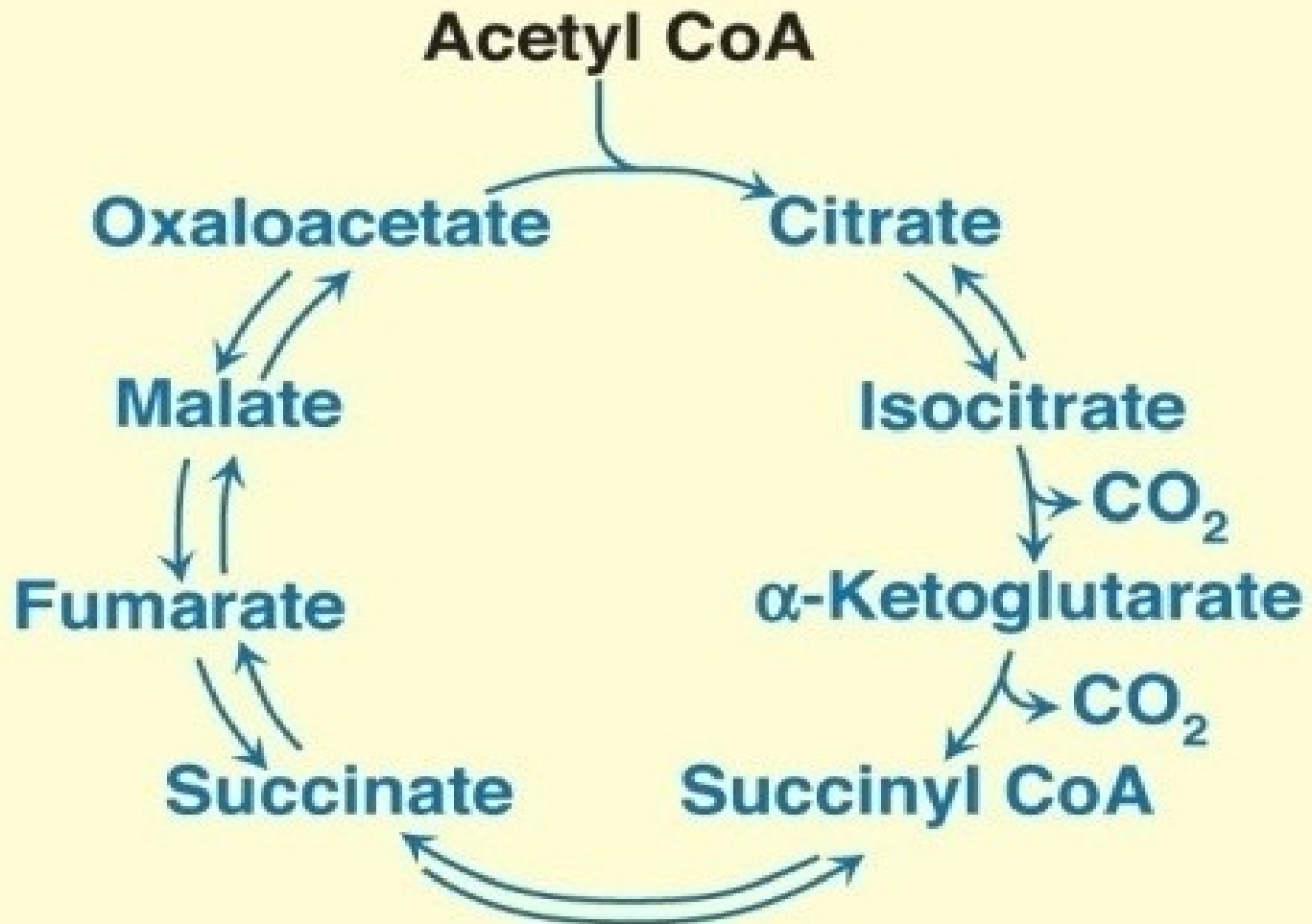


Krebs Cycle



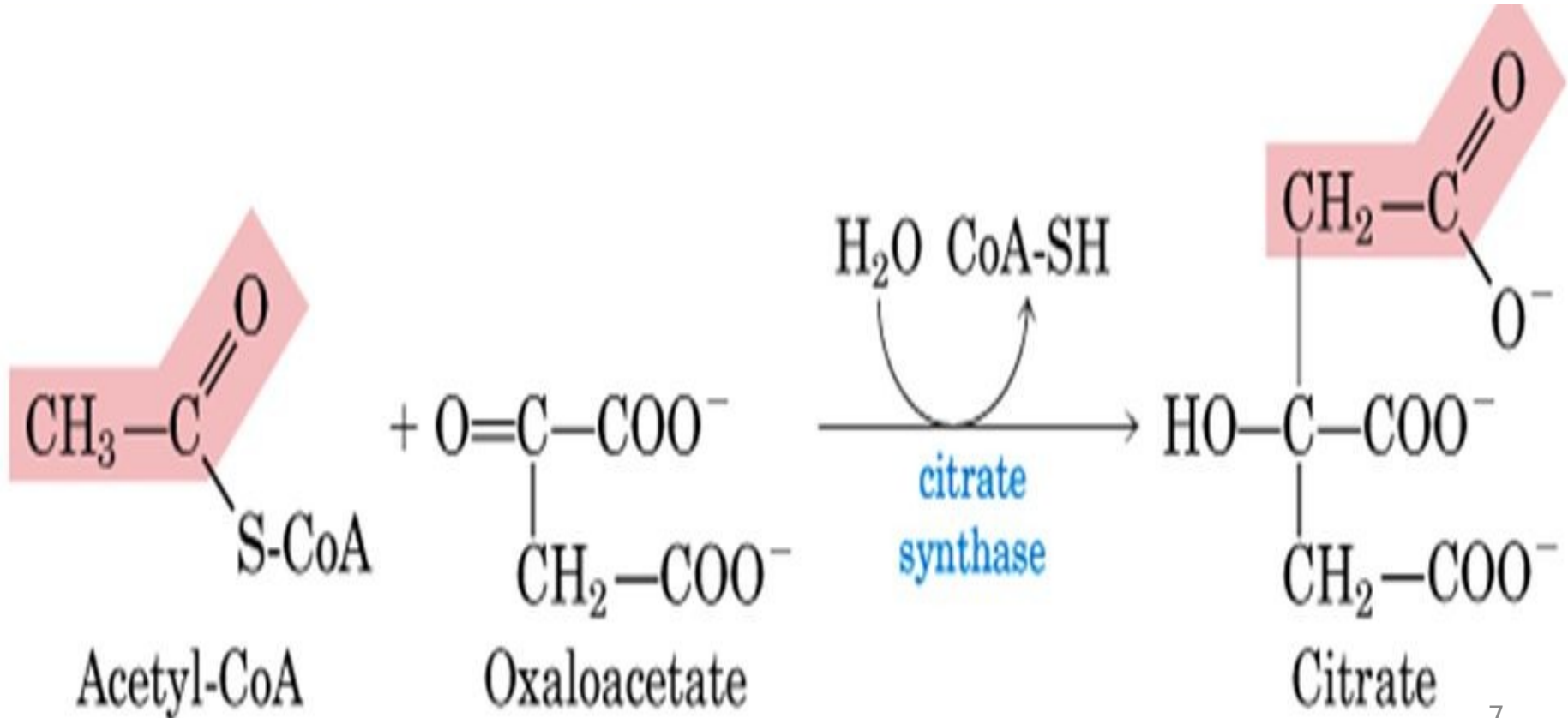
Is a series of reaction that occurs in aerobic cells Order to make complete oxidation of **AcetylCoA** derived from carbohydrates, fats, and proteins into **CO₂** & chemical energy in the form of (**ATP**)

Krebs Cycle



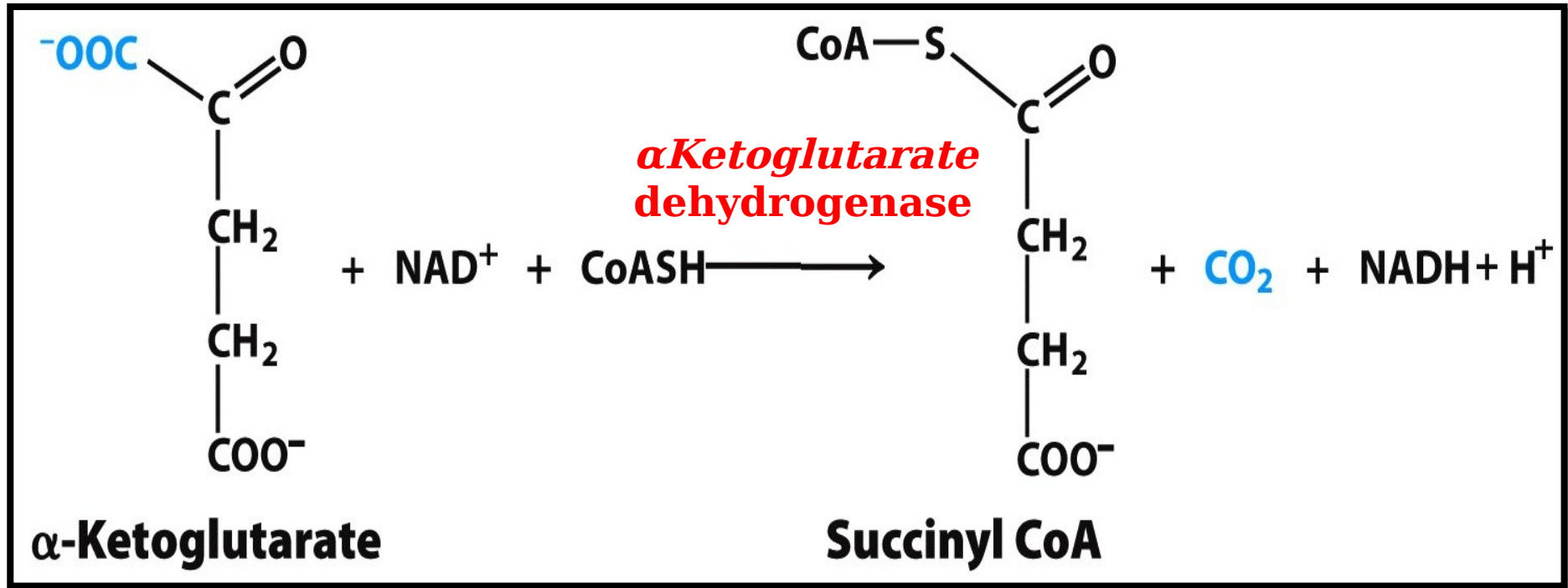
Citrate Synthase

Condensation of acetyl CoA and oxaloacetate to form citrate



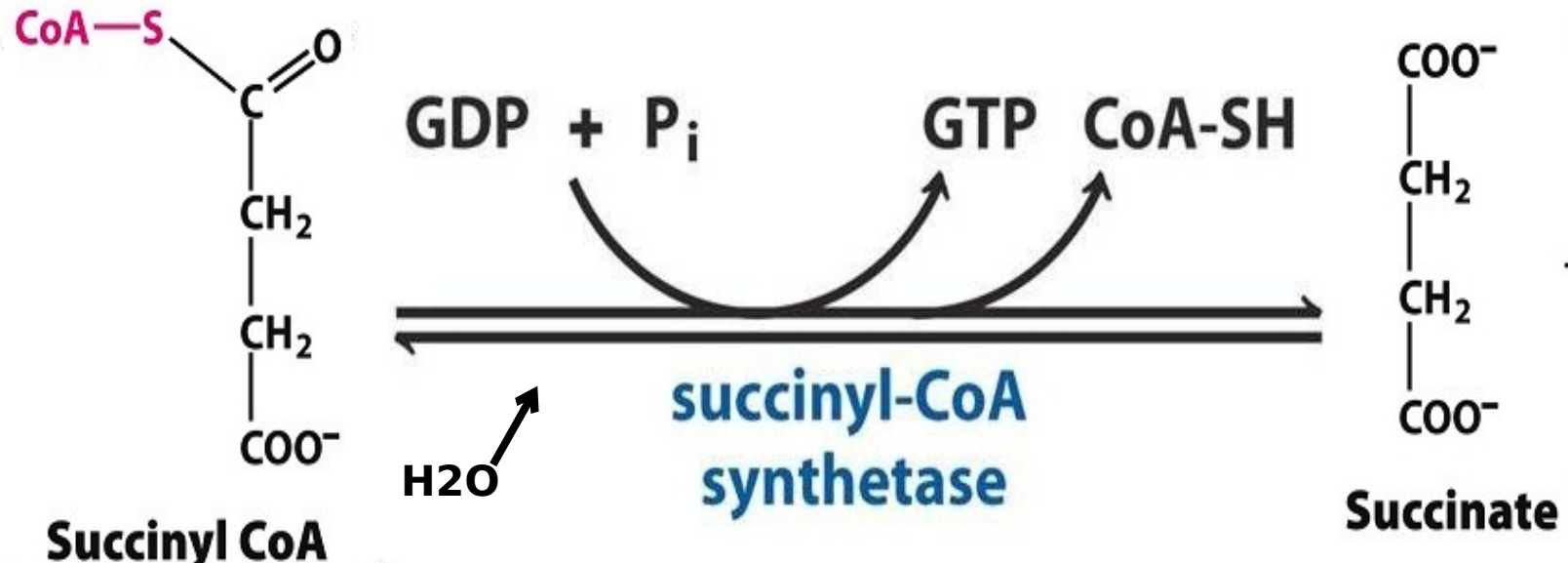


α Ketoglutarate Dehydrogenase



**It is enzyme for Oxidative decarboxylation
(Typical as PDH) BUT Does Not Subjected
to Covalent Modification Like PDH.**

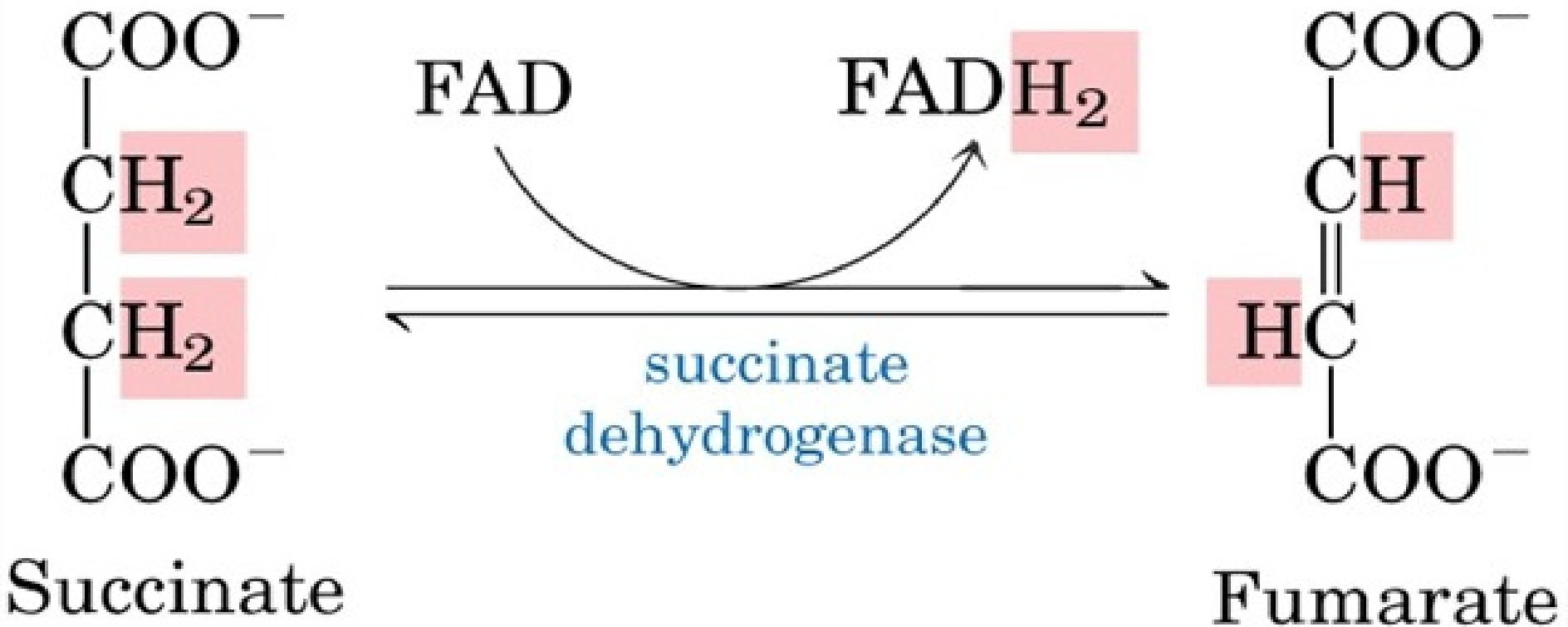
Succinate Thiokinase = Succinyl-CoA Synthetase



In this reaction the energy rich thioester linkage is hydrolyzed with release of energy that is conserved in

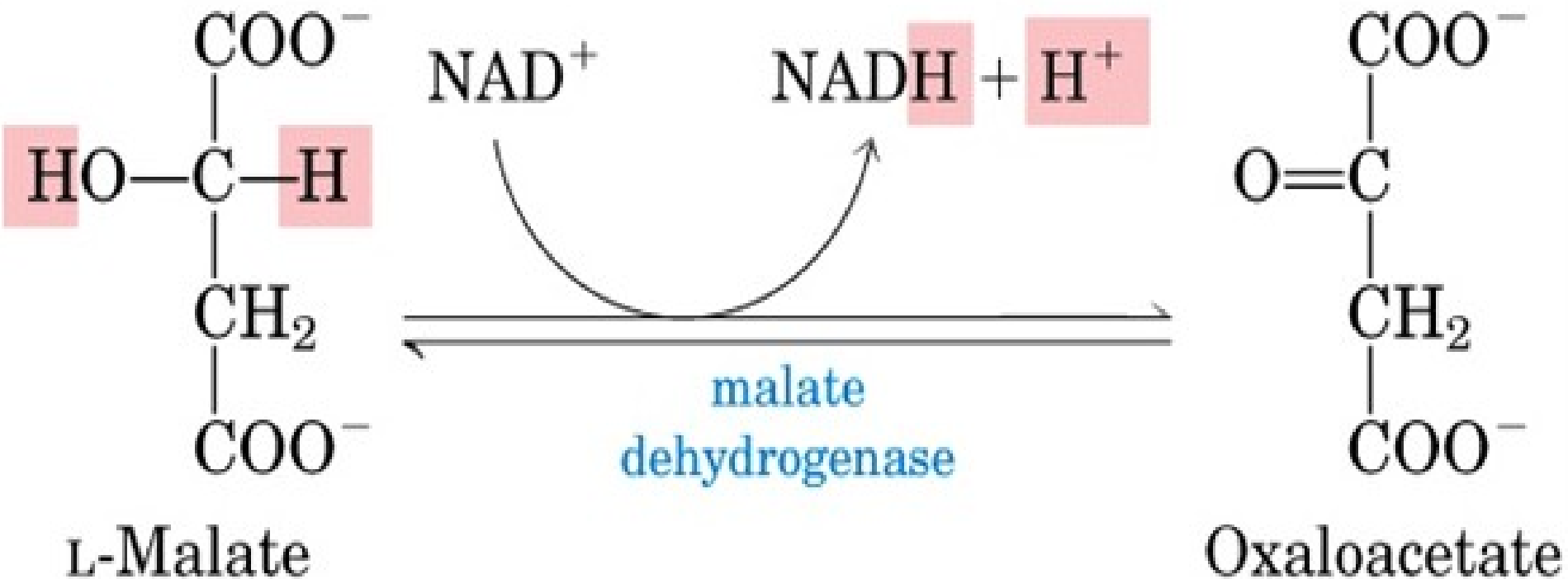
substrate level of phosphorylation of GDP to GTP

Succinate Dehydrogenase



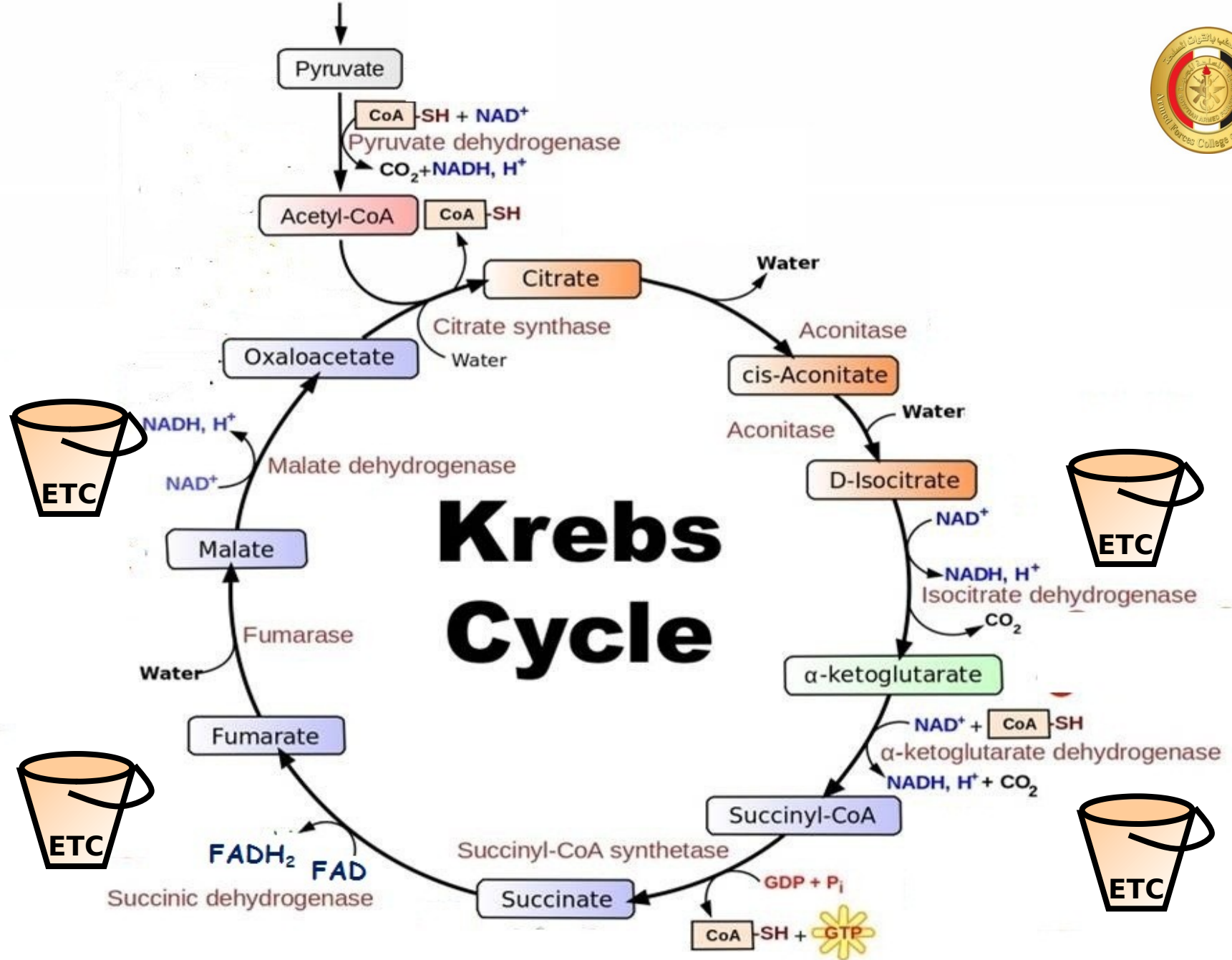
Succinate dehydrogenase is competitively inhibited by malonate

Malate Dehydrogenase (MD)



SO!

Oxaloacetate is regenerated at end of cycle





Energy Yield Of The TCA??

$$\text{TCA} = 3 (\text{NADH}) + 1 (\text{FADH}_2) + 1 \text{ ATP}$$

$$= 3 \times 3 + 1 \times 2 + 1$$
$$= 12 \text{ ATP}$$



To summarize

in TCA the **2 carbons of acetyl CoA**
are
oxidized and released in the form
of **CO₂**, with concomitant
formation of

How many molecules of ATP are produced by complete oxidation of one glucose molecule aerobically??

- Glycolysis= 8
- 2 PDH= 6 ATP
- TCA = 3 (NADH)+ 1 (FADH₂)+ 1 ATP

$$3 \times 3 + 1$$

$$1 + 2 + 9 =$$

$$\text{ATP/ 1 AcetylCoA } 12 =$$

$$\text{Acetyl CoA} = 12 \times 2 = 24$$

$$= 8 + 6 + 24$$



38 ATP

The FADH₂ and NADH produced by the oxidation of one acetyl-CoA result in the synthesis of about --- ATPs



- A.10
- B.11**
- C.15
- D.20
- E.7



The reaction succinyl CoA to succinate requires



1. FAD
2. ATP
3. GDP
4. NADP
5. NAD





Biological Importance of TCA = **Amphibolic Nature of TCA**

(Its relation to other pathways)

□ Catabolic (oxidative) Nature Of TCA Cycle

“Convergent ”

Glucose



Pyruvate

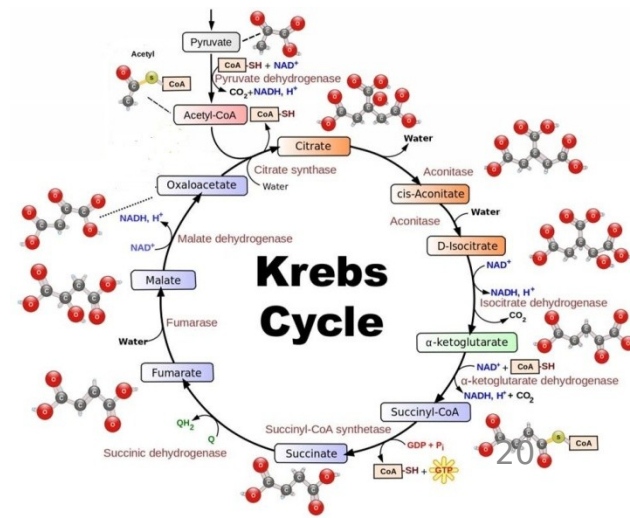


Acetyl CoA

Fatty acids oxidation

Ketone bodies by ketolysis

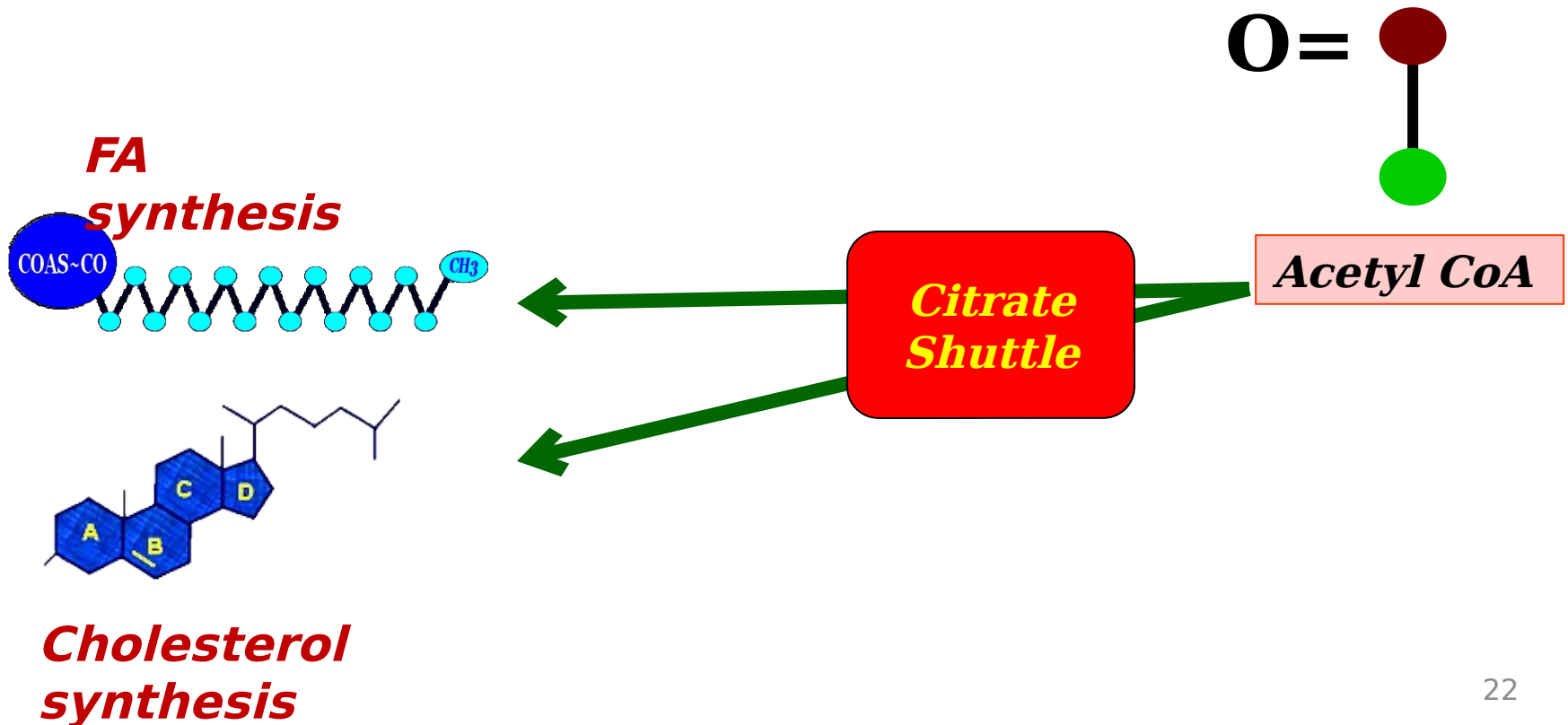
Some aminoacids catabolism
(ketogenic)

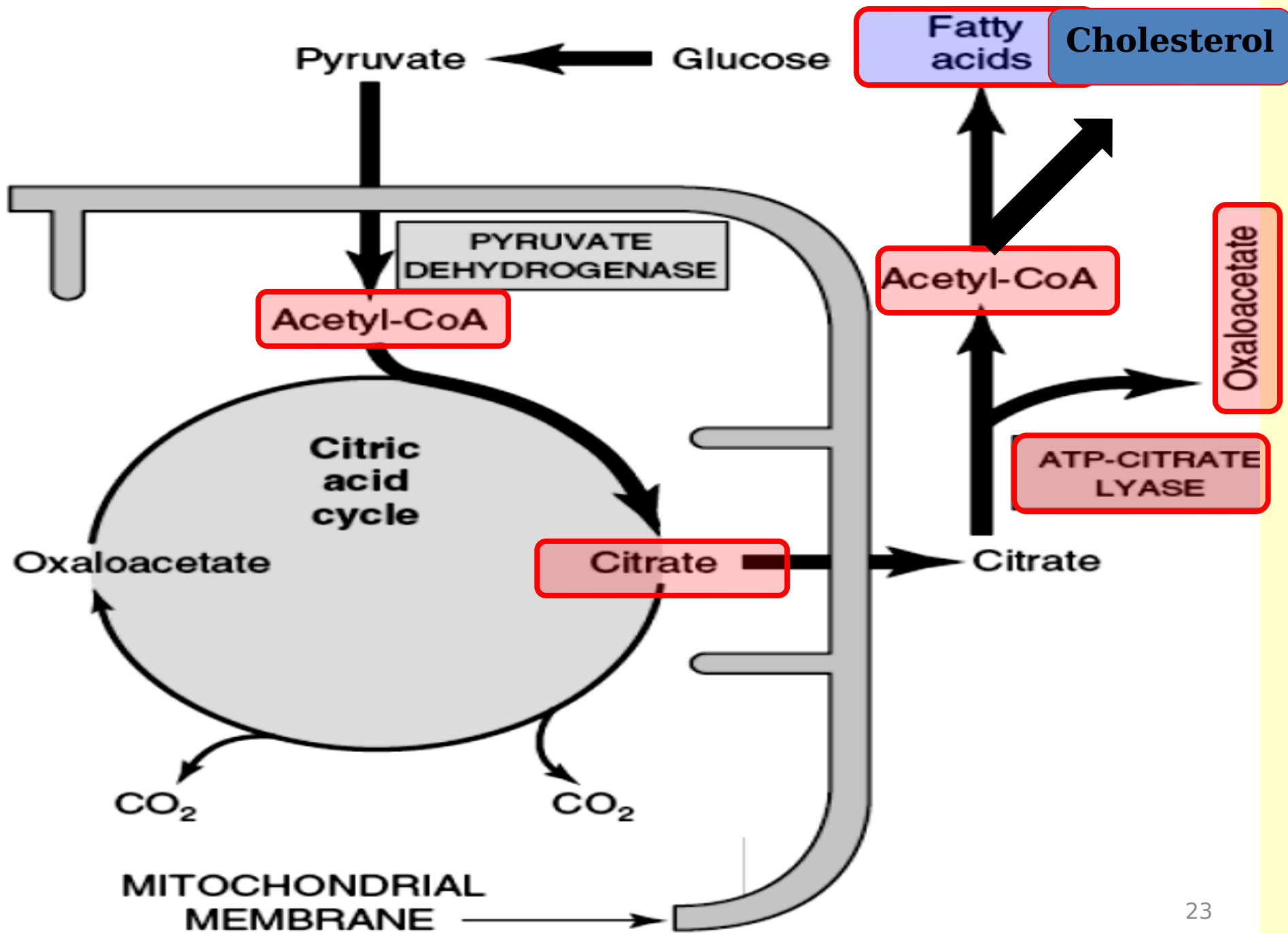




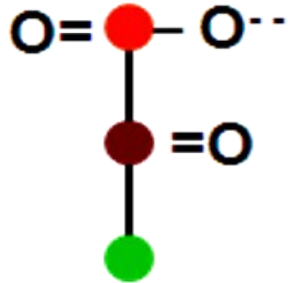
Anabolic Nature Of The TCA Cycle (Divergent)

1. FA & Cholesterol Synthesis

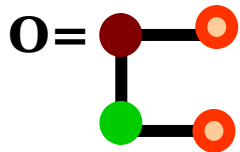
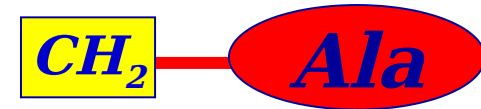
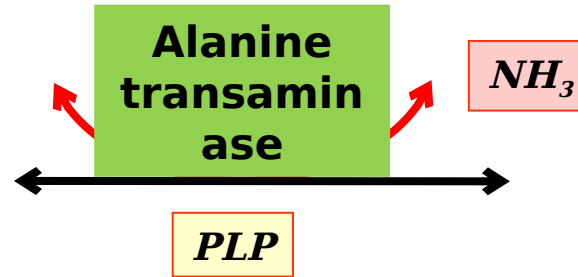




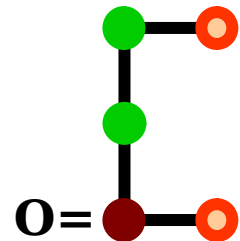
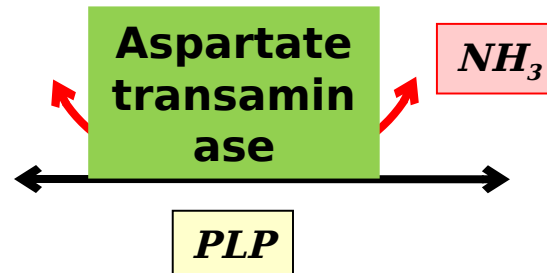
2. Non Essential a.a Synthesis (Transamination)



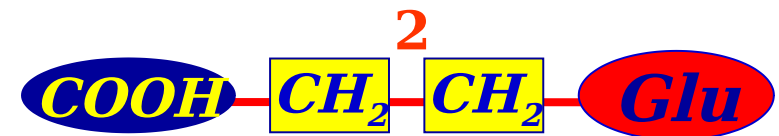
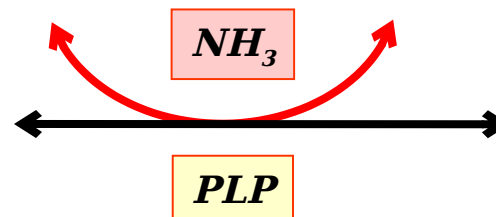
Pyruvate



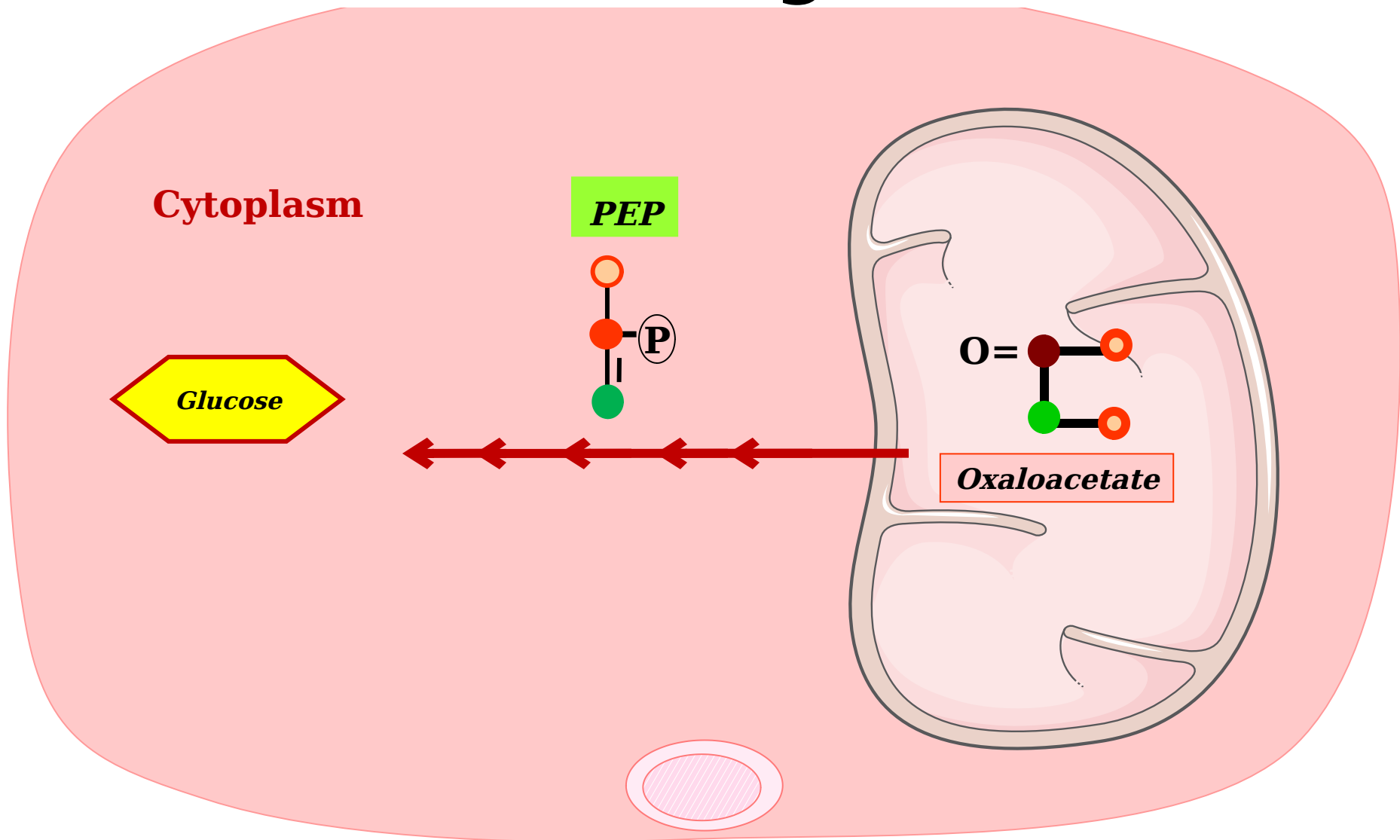
Oxaloacetate



α Ketoglutarate



3. Synthesis Of Glucose (Gluconeogenesis)

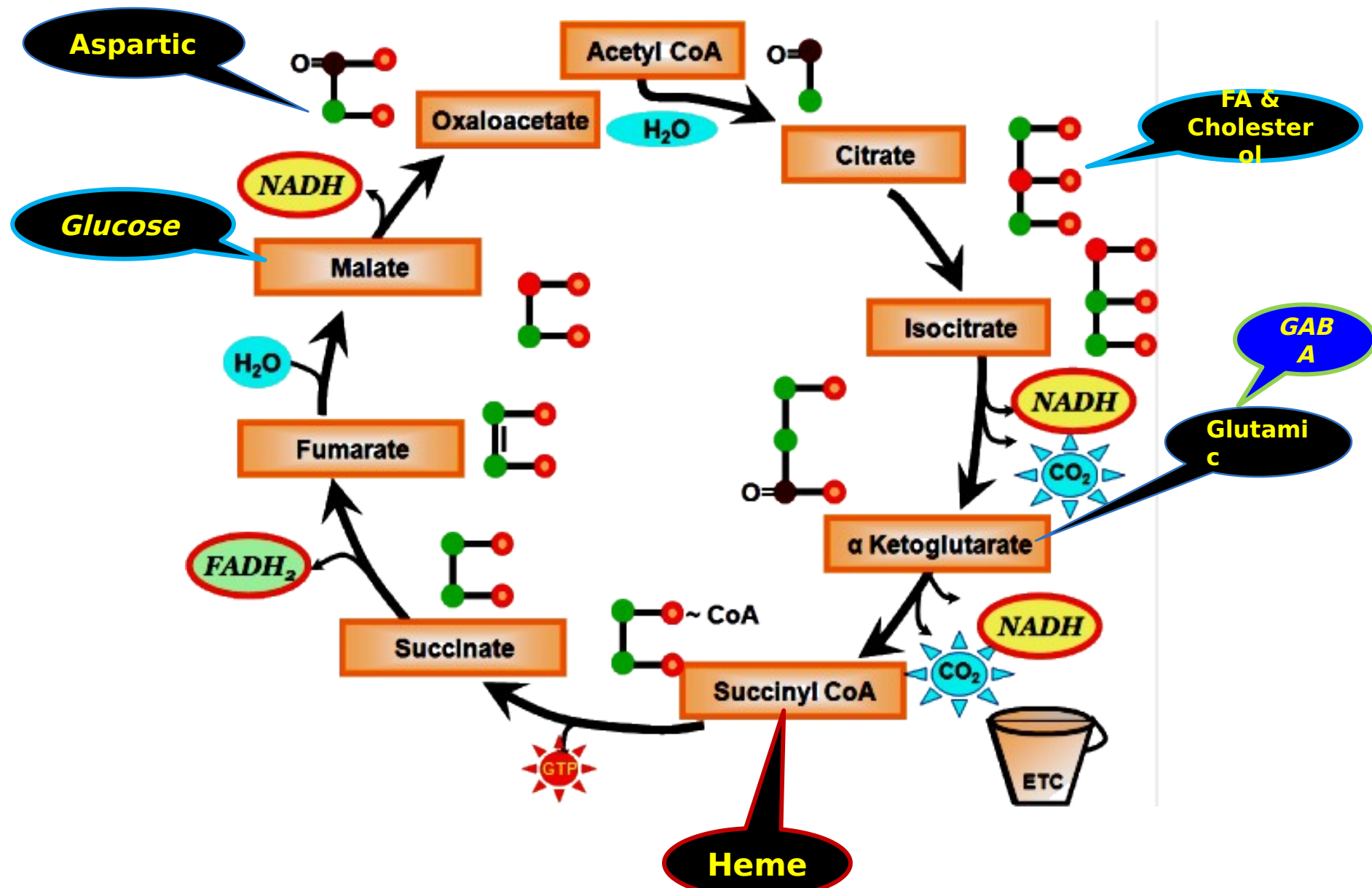




4.Synthesis Of Heme

Succinyl CoA $\longrightarrow$ $\longrightarrow$ **Heme**

Efflux Of TCA Cycle Intermediates“Divergent ”



An anaplerotic reaction which sustains the availability of oxaloacetate is the carboxylation of



- 1. Glutamate**
- 2. Citrate**
- 3. Pyruvate**
- 4. Succinate**

Which of the following statements regarding TCA cycle is true?



- 1. It is an anaerobic process**
- 2. It occurs in cytosol**
- 3. It contains no intermediates for Gluconeogenesis**
- 4. It is amphibolic in nature**



Take Home Message

:Krebs cycle

**Final common pathway for the -
oxidation of carbohydrates, fatty acids
and amino acids**

occurs in the mitochondria -

Aerobic and amphibolic -

**Mainly catabolic, with some anabolic -
features**

**The complete oxidation of one glucose -
molecule results in a net production of
38 ATP molecules**

Important Note



There are many Other sources for Acetyl CoA.

- **Glycolysis (wel fed state)**
- **FA Oxidation, Ketolysis & Ketogenic a.a (Fasting State).**

So TCA Cycle CAN CONTINUE in both well fed & fasting state

SUGGESTED TEXTBOOKS



- ✕ "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R.Ferrier
- ✕ "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W.Rodwell.
- ✕ Fundamentals of Clinical Chemistry (Tietz) Sixth
- ✕ "Textbook of Biochemistry with Clinical Correlations" by T.M.Devlin
- ✕ www.namrata.co- ***Biochemistry for medics***

Thank you!

